Appl. No. 10/621,623

Amdt. Dated July 25, 2006

Reply to Office action of January 25, 2006

IN THE CLAIMS

1. (*Withdrawn*) A method of making 2-butyl-3-[2'-(triphenylmethyltetrazol-5-yl)-biphenyl-4-yl methyl]-1,3-diazaspiro[4.4]non-1-ene-4-one comprising the step of reacting 2-butyl-1,3-diaza-spiro[4.4]non-1-ene-4-one and 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1*H*-tetrazole in the presence of a phase transfer catalyst in a reaction system comprising first and second phases.

- 2. (Withdrawn) The method of claim 1 wherein the first phase comprises an aromatic or aliphatic hydrocarbon and the second phase comprises water.
- 3. (Withdrawn) The method of claim 2 wherein, prior to reaction, the 2-butyl-1,3-diazaspiro[4.4]non-1-ene-4-one is in solution in aqueous base.
- 4. (Withdrawn) The method of claim 3 wherein the aqueous base is selected from the group consisting of KOH, NaOH and LiOH.
- 5. (Withdrawn) The method of claim 4 wherein the aqueous base is aqueous KOH.
- 6. (Withdrawn) The method of claim 2 wherein, prior to reaction, the 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1H-tetrazole is in solution in an aromatic or aliphatic hydrocarbon.
- 7. (Withdrawn) The method of claim 6 wherein the 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1*H*-tetrazole is in solution in an aromatic hydrocarbon that is toluene.
- 8. (Withdrawn) The method of claim 2 wherein the 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1*H*-tetrazole is in solution in an aliphatic hydrocarbon.

Appl. No. 10/621,623
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- 9. (Withdrawn) The method of claim 1 wherein the phase transfer catalyst is a quaternary ammonium compound.
- 10. (Withdrawn) The method of claim 9 wherein the quaternary ammonium compound is tetrabutyl ammonium hydrogensulfate.
- 11. (Presently Amended) A method for making irbesartan comprising the steps of:
 preparing 2 butyl 3 [2' (triphenylmethyltetrazol 5 yl) biphenyl 4 yl methyl] 1,3diazaspiro[4.4]non-1-ene-4-one prepared according to the method of claim 1; combining 2butyl-1,3-diaza-spiro[4.4]non-1-ene-4-one and 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1Htetrazole in the presence of a phase transfer catalyst in a reaction system comprising first and
 second phases; heating the combination to a temperature of about 20° C and about 95° C;
 separating the first and second phases; removing solvent from the first phase to obtain a
 residue; providing a mineral or sulfuric acid acidified solution of the residue in a watermiscible solvent, basifying the solution in water-miscible solvent with an inorganic base;
 removing water-miscible solvent from the solution; separating trityl alcohol so formed; and
 recovering irbesartan.
- 12. (Original) The method of claim 11 wherein the water miscible solvent is acetone.
- 13. (Original) The method of claim 11 wherein the basification is with an inorganic base to a pH of about 8 to about 12.
- 14. (Original) The method of claim 13 wherein basification with inorganic base is to a pH of about 9 to about 10.5.
- 15. (Original) In a method of making irbesartan, the step of combining, in the presence of a phase transfer catalyst, a solution of 5-(4'-bromomethylbiphenyl-2-yl)-1-trityl-1H-tetrazole in a first solvent that is an aromatic or aliphatic hydrocarbon and a solution of 2-butyl-1,3-

Appl. No. 10/621,623Amdt. Dated July 25, 2006Reply to Office action of January 25, 2006

diazaspiro[4.4]non-1-ene-4-one in a second solvent comprising water and an inorganic base, whereby first (organic) and second (aqueous) phases are formed.

- 16. (*Presently Amended*) The method of claim 15 wherein the <u>first solvent aromatic or aliphatic hydrocarbon</u> is the aromatic hydrocarbon toluene.
- 17. (Original) The method of claim 15 wherein the phase transfer catalyst is tetrabutylammonium hydrogensulfate.
- 18. (Original) The method of claim 15 wherein the inorganic base is KOH.